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Mechanically Adaptive Silicon-based Neural Probes for Chronic High-resolution Neural Recording

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Abstract

A hybridly assembled, neural probe based on silicon (Si) with reduced dimensions and improved mechanical flexibility is proposed as a chronic neural interface. In contrast to previous approaches, the microelectrode array at the probe tip will be completely implanted into cortical tissue and tethered only by a slender and highly flexible, 11-µm-thick polyimide cable. The Si-based electrode arrays carry 16 or 32 channels and feature cross-sections as small as $50 \times 120\ \mu m^2$ across their entire length. Implantation of the flexible probes is facilitated by a temporary increase in probe stiffness using a bio-dissolvable polymer coating. The centrifuge-based molding of polyethylene glycol creates sharp insertion vehicles with a thickness of only 75 µm. Probe implantation up to 9 mm into agar-based brain models demonstrates the insertion capability of the novel mechanically adaptive neural probes.

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Keywords: Microelectrode array; Intracortical neural probe; Flexible substrate; Biodegradable materials; Polyethylene glycol; Molding; Silicon

1. Introduction

The optimization of the mechanical and geometrical properties of neural interfaces implanted into cortical tissue is a highly relevant research topic in the field of neural engineering. The host tissue response to the implanted foreign body ultimately results in a loss of recording capability related, among other causes, to an increase in the functional

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distance between the implant and neuronal cell bodies. It has been shown that small neural implants floating in the cortical tissue elicit significantly less adverse effects than larger, rigidly tethered implants [1].

Most approaches for shaft probes rely either on stiff silicon [2] or on flexible polymer substrates [3,4], the latter being based mainly on polyimide (PI) or parylene-C. Although the flexibility of polymer probes is an advantage, they usually feature a lower channel number and recording site density. Further, these devices lack the CMOS-compatibility of Si probes, which offers electronic control of the location of the recoding sites to improve signal quality and stability [5].

We present a concept for a hybridly assembled neural probe composed of a long, slender PI ribbon cable and a minute Si probe tip carrying a dense microelectrode array. In contrast to established Si-based systems {Fig. 1(a)}, the novel probe benefits of a substantial reduction of the probe/cable interface area that is now closer to the tip region of the probe and is also implanted in the cortical tissue {Fig. 1(b)}. The Si substrate of the probe tip lends itself for CMOS integration in future versions. For implanting the flexible probe, a bio-dissolvable coating is precisely shaped around the assembly {Fig. 1(c)}. This so-called insertion vehicle will dissolve shortly after implantation and restore the flexibility of the interconnect, making the probe mechanically adaptive.

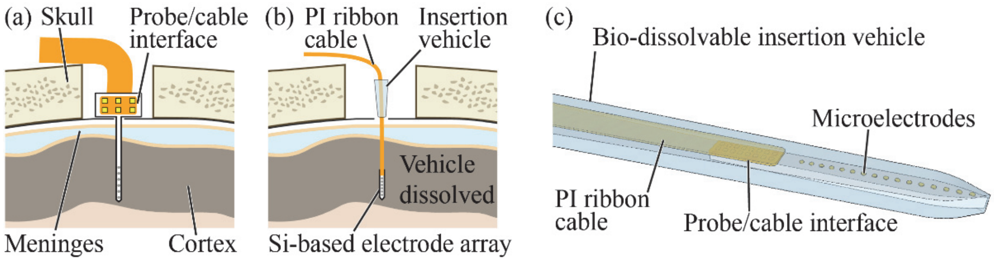

Figure 1: Schematic of (a) conventional and (b) flexible, hybridly assembled probe, and (c) flexible probe with insertion vehicle.

2. Fabrication

2.1. Probe components and hybrid assembly

Implementing the slender probe as proposed in Fig. 1(b,c) requires the miniaturization of the main components of Si-based neural probes, namely the electrode array at the probe tip {Fig. 2(a)} and the interfacing PI cable {Fig. 2(b)}. The miniaturization is limited mainly by the dimensions of the probe/cable interface required for flip-chip assembly. Electrode arrays with 16 or 32 channels and a minimal width and length of 120 µm and 1.3 mm, respectively, were realized. A CMOS-compatible MEMS process involving deep reactive ion etching (DRIE) and wafer rear grinding serves to release 50-µm-thick electrode arrays from standard Si substrates [6]. The PI cable comprises two sputter deposited platinum metallization layers sandwiched between three spin-coated PI layers (U-Varnish S, UBE Industries Ltd., Tokyo, Japan). The interconnecting wires are patterned in a dry etching process. Figure 2 (c) compares an assembled test structure of the flexible probe to a conventional probe.

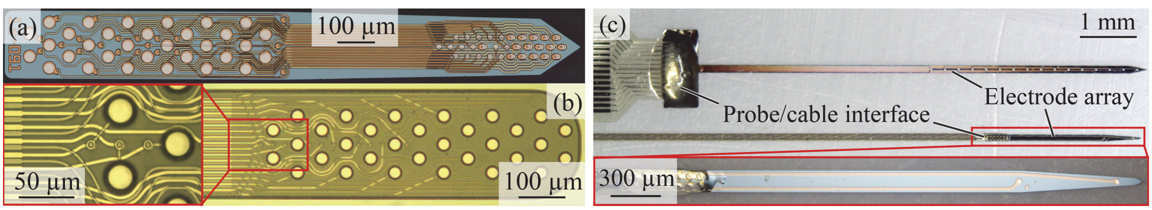

Figure 2: Micrographs of 32 channel (a) electrode array and (b) PI cable; (c) Comparison between conventional (top) and slender probe.

2.2. Probe stiffening

Figure 3 outlines the fabrication of the mold for PEG shaping according to the cut along A-A' indicated in the photograph of the mold shown in Fig. 4. The fabrication starts with the patterning of 75-µm-thick dry resist layers (Ordyl Alpha 375, Elga Europe s.r.l, Milan, Italy) that are laminated to HMDS-treated 4" Si substrates {Fig. 3(a-c)}. Subsequently, 3D printed structures are adhesively bonded to the Si and the photoresist {Fig. 3(d)}. These structures later define vias and a central reservoir in the mold (cf. Figs. 3 and 4). The resulting component is then repeatedly used to pattern silicone rubber (Elastosil M 4600, Wacker Chemie AG, Munich, Germany). The HMDS treatment ensures that the rubber does not permanently bond to the silicon substrate. After peeling off the patterned rubber disc, the neural probes are placed inside the open trenches {Fig. 3(f)}. Subsequently, the channels and cavities are buried using a plain disk made of the same rubber. The adhesion between the two rubber components is strong enough for the following PEG molding, but still allows to remove the cap after finishing the stiffening process.

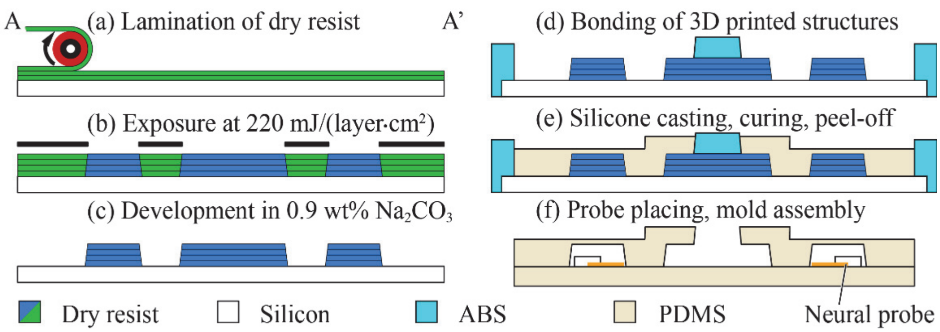

Figure 3: Schematic fabrication process of mold for probe stiffening; cross-sectional view along line A-A' in Fig.6 (a).

The flexible probes inside the mold cavities were stiffened using channels with a height of 75 µm and 225 µm and PEG-1500 (Merck Chemicals GmbH, Schwalbach, Germany). The polymer is molten and dispensed into the reservoirs of the mold at 75 °C. The molds are then centrifuged on a spin coater at 2000 rpm and the PEG spreads into the probe cavities {cf. Fig. 4(a)}. Finally, the molds are annealed and slowly cooled to room temperature, eliminating constrictions otherwise occurring at the grain boundaries of the PEG (Fig. 4 b). The resulting insertion vehicles are homogeneous and fine-grained, as show in Fig 4(c). Due to the placement of the probes inside the molds with the electrode attached to the rubber, the majority of the coating is located at the back of the probes, leaving only a thin PEG layer on the electrode surfaces.

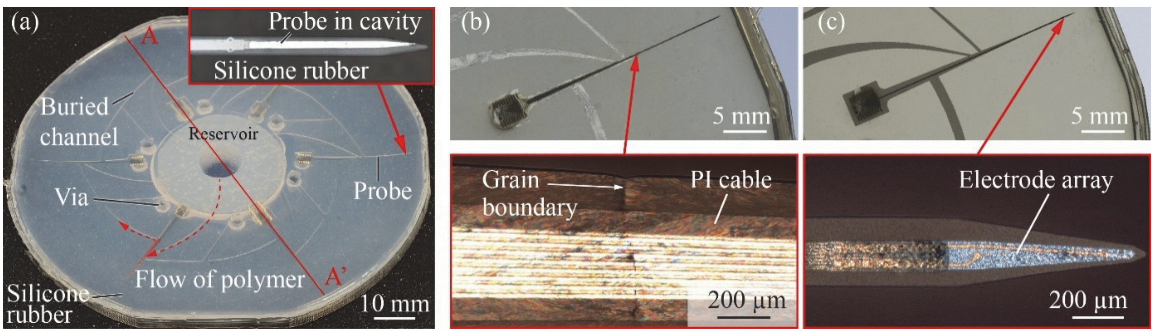

Figure 4: (a) Photograph of centrifuge mold after assembly, inset showing micrograph of a probe cavity. Photographs of centrifuge molds after PEG coatingp, (a) before and (b) after the annealing step.

3. Insertion Experiment

Agar-based brain models are used to validate the insertion capability of the mechanically adaptive neural probes {Fig. 5(a-d)} [7]. For these tests, probes were attached to a custom-made insertion tool with a vacuum chuck. A linear motor descended the probes into the brain model orthogonally to the agar gel surface. Probes encased in 75-µm-thick PEG vehicles were implanted to a maximum depth of 9 mm at a speed of 10 mm/s. After retracting the probes from the gel, the PEG layer was dissolved, after which a second implantation of the same probe failed, demonstrating the necessity of the temporary stiffening for implanting the highly flexible probes {Fig. 5(e)}.

A time-resolved impedance spectroscopy in a conductive agar gel prepared with 1 M Ringer's solution demonstrates that stable electrode impedances are reached 1 min after implantation. The average, minimum and maximum value of the electrode impedance at 1 kHz of four electrodes on probes with 225-µm-thick PEG coatings are plotted in Fig. 5(f) over the course of 80 s.

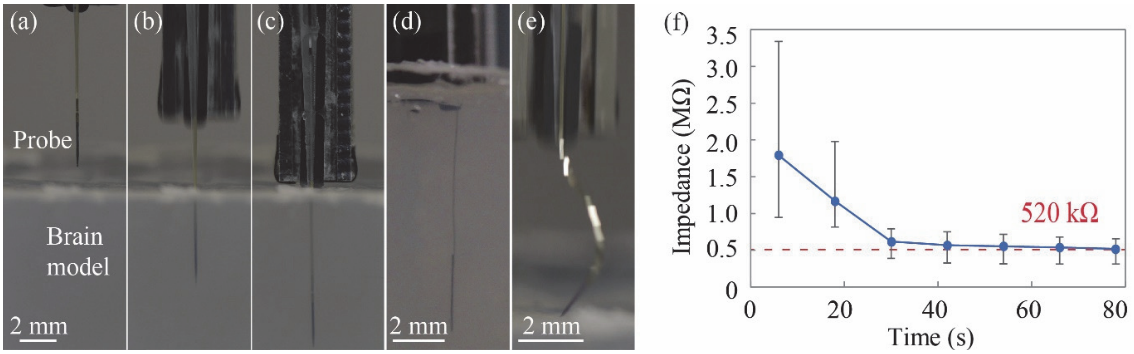

Figure 5: Photographs of PEG-stiffened probe in insertion experiment shown (a-c) perpendicular and (d) in-plane to the electrodes. (e) After PEG dissolution, a repeated implantation of the flexible probe fails. (f) Time-resolved impedance of four stiffened probes during PEG dissolution.

4. Conclusion

The novel, mechanically adaptive neural probe features a fully implantable Si-based probe tip that allows CMOS-based high-density arrays to be integrated while the highly flexible PI cable enables the floating operation of the Si probe in the brain tissue in chronic experiments. Insertion vehicles composed of 75-µm-thick PEG casts implemented in a novel coating scheme allow deep and precise probe implantation with minimal overhead in probe volume. The probes allow to interface cortical regions in depths of at least 9 mm while exerting minimal forces on the host tissue.

Acknowledgements

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